

PATENT COOPERATION TREATY

RECEIVED

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
 JOHN W. WALLEN, III  
 JOHNSON & JOHNSON  
 ONE JOHNSON & JOHNSON PLAZA  
 NEW BRUNSWICK, NJ 08933-7003

*Search Response  
 4-12-02*

PCT FEB 19 2002

NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL SEARCH REPORT  
 OR THE DECLARATION

(PCT Rule 44.1)

*SA/TW*

Date of Mailing  
 (day/month/year) **12 FEB 2002**

Applicant's or agent's file reference ORT-1489-PCT	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/US01/26373	International filing date (day/month/year) 24 August 2001 (24.08.2001)
Applicant ORTHO-MCNEIL PHARMACEUTICAL, INC.	

1.  The applicant is hereby notified that the international search report has been established and is transmitted herewith.  
 Filing of amendments and statement under Article 19:  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):  
  
 When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompany sheet.  
  
 Where? Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35  
  
 For more detailed instructions, see the notes on the accompanying sheet.
2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
  - the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
  - no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. Further action(s): The applicant is reminded of the following:  
  
 Shortly after 18 months from the priority date, the international application will be published by the International Bureau.  
 If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.  
  
 Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).  
  
 Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Gailene R. Gabel Telephone No. (703) 308-0196
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*Gailene R. Gabel  
 for*

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From the INTERNATIONAL SEARCHING AUTHORITY

To:  
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## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

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International application No.  
 PCT/US01/26373

International filing date  
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Name and mailing address of the ISA/US  
 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231  
 Facsimile No. (703)305-3230

Authorized officer  
 Gailene R. Gabel *Gailene R. Gabel*  
 Telephone No. (703) 308-0196

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ORT-1489-PCT	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US01/26373	International filing date ( <i>day/month/year</i> ) 24 August 2001 (24.08.2001)	(Earliest) Priority Date ( <i>day/month/year</i> ) 06 September 2000 (06.09.2000)
Applicant ORTHO-MCNEIL PHARMACEUTICAL, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (See Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. 1

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

None of the figures

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/26373

Box III TEXT OF THE ABSTRACT (Continuation of Item 5 of the first sheet)

NEW ABSTRACT

The present invention relates to a method for monitoring the effect of in vivo administration of cathepsin S inhibitors by measuring accumulation of an intermediate degradation product of invariant chain (Ii), in particular the p10 Ii fragment, in blood of dosed patients. See Figure 1.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US01/26373

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>				
IPC(7) : G01N 33/535, 33/545				
US CL : 435/7.24				
According to International Patent Classification (IPC) or to both national classification and IPC				
<b>B. FIELDS SEARCHED</b>				
Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/7.2, 7.21, 7.23, 7.71, 7.92, 173.4, 173.7, 173.9, 287.7, 964; 436/507, 508, 519, 172, 813; 424/9.2				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched				
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) MEDLINE, EMBASE, SCISEARCH, BIOSIS				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	WO 99/58153 A1 (BRIGHAM & WOMEN'S HOSPITAL) 18 November 1999	1-3		
--	(18.11.1999), see entire document, especially pages 13-17.	-----		
Y		4		
Y	WO 97/40066 A1 (MASSACHUSETTS INSTITUTE of TECHNOLOGY) 30 October 1997	1-4		
	(30.10.1997), see entire document, especially pages 7-18.			
A/P	US 6,245,904 B1 (MELMS et al.) 12 June 2001 (12.06.2001), see entire document.	1-4		
A	US 5,919,639 A (HUMPHREYS et al.) 06 July 1999 (06.07.1999), see entire document.	1-4		
Y	SHI G.P. et. al. Role for cathepsin F in invariant chain processing and major histocompatibility complex class II peptide loading by macrophages. Journal of Experimental Medicine. April 2000, vol. 191, No. 7, pages 1177-1186, see abstract.	1-4		
Y	Database Medline ACCN. No. 1999:170289. Impaired invariant chain degradation and antigen presentation and diminished collagen-induced arthritis in cathepsin S null mice. Immunity. NAKAGAWA et al., see abstract, February 1999.	1-4		
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.				
* Special categories of cited documents: <table border="0" style="width:100%"> <tr> <td style="width:50%">               "A" document defining the general state of the art which is not considered to be of particular relevance                "E" earlier application or patent published on or after the international filing date                "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)                "O" document referring to an oral disclosure, use, exhibition or other means                "P" document published prior to the international filing date but later than the priority date claimed             </td> <td style="width:50%">               "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention                "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone                "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art                "&amp;" document member of the same patent family             </td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family			
Date of the actual completion of the international search		Date of mailing of the international search report		
16 November 2001 (16.11.2001)		<b>12 FEB 2002</b>		
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230		Authorized officer Gailene R. Gabel <i>Janice Ford for</i> Telephone No. (703) 308-0196		

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the letter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

**What parts of the international application may be amended ?**

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

**When ?** Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

**Where not to file the amendments ?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/s filed, see below.

**How ?** Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

**What documents must/may accompany the amendments ?**

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.